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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/896,812	06/29/2001	Thomas D. Madden	16303-008030	6998

500 7590 03/09/2005

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EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 03/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/896,812	MADDEN ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32,34-36,38-41,43-48 and 64-67* is/are pending in the application.

4a) Of the above claim(s) *44-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32,34-36,38-41 and 64-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The RCE filed on 1-25-05 is acknowledged.

Claims included in the prosecution are 32, 34-36, 38-41 and 64-67. Claims 44-48 remain withdrawn from consideration.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 32, 34-35, 39-41, 43 and 67 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims1-2, 4-5 and 17 of copending Application No. 09/896,811. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims in instant application and the copending application are drawn to liposomal compositions containing camptothecin, sphingomyelin and cholesterol. Instant claims are generic with respect to the dosages and the drug lipid ratios and therefore deemed to include these specific limitations recited in the claims of said copending

application. The claims in said copending application are generic with respect to the amount of the precipitated drug in instant claims and therefore, deemed to include instant limitations

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

4. Claims 32 and 34-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Madden et al (Proc.of ASCO, 1998) of record.

Madden et al disclose liposomal formulations containing sphingomyelin and cholesterol. The aqueous interior contains Topotecan (abstract). Although Madden et al explicitly state that Topotecan is in at least 50 % precipitated form, such is implicit in view of the fact that the compound is extremely insoluble in water and Madden's liposomes contain the drug in the aqueous interior.

That camptothecins are extremely insoluble in aqueous solutions is evident from WO 99/13816, which is already of record (page 2, lines 6-7).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 39-41, 43 and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Madden et al cited above.

As pointed out above, Madden et al disclose liposomal formulations containing sphingomyelin and cholesterol. The aqueous interior contains Topotecan. Although Madden et al explicitly state that Topotecan is in at least 50 % precipitated form, such is implicit in view of the fact that the compound is extremely insoluble in water and Madden's liposomes contain the drug in the aqueous interior.

The abstract of Madden et al does not provide any details as to the drug-lipid ratios or the sphingomyelin-cholesterol ratios. Assuming that they are different, it is deemed obvious to one of ordinary skill in the art to manipulate these ratios to obtain the best possible results.

7. Claims 32, 34-36, 38-41 and 64-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kirpotin (6,110,491) by itself or in combination with Webb (5,543,152).

Kirpotin as also pointed out in the previous action, discloses liposomal compositions wherein the active agent is in the precipitated form. The active agent according to Kirpotin can be any compound with ionizable groups. The active agents suggested by Kirpotin are antineoplastic agents, doxorubicin, vincristin, vinblastine and others. The liposomes are made of various phospholipids and sphingomyelin; the liposomes contain cholesterol. The lipid - drug ratios in Kirpotin also appear to fall within the claimed ratios (abstract; col. 4, line 54 through col. 6, line 18; col. 9, lines 22-67; examples and claims). Kirpotin's examples include only liposomes made from egg phosphatidylcholine and cholesterol in amounts falling within claimed ratios and not sphingomyelin; however, it would have been obvious to one of ordinary skill in the art to use sphingomyelin instead of phospholipid in the liposomes since Kirpotin is suggestive of the use of sphingomyelin and provides guidance as to how to make these liposomes. The use of sphingomyelin along with cholesterol would also have been obvious to one of ordinary skill in the art since Webb teaches several advantages of liposomal formulations based on sphingomyelin and cholesterol (in instant amounts). According to Webb, these liposomes are much more stable to acid hydrolysis, significantly better drug retention characteristics, better loading characteristics into tumors and Webb teaches the applicability of the liposomes to a variety of lipophilic drugs, vinca alkaloids in particular (abstract, col. 4, line 18 through col. 5, line 34, examples and claims). Although both Kirpotin, and Webb lack the specific teachings of camptothecins, it would have been obvious to one of ordinary skill in the art to use any lipophilic drug including camptothecins with a reasonable expectation of

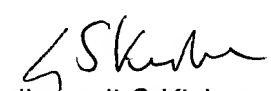
success since both teach the applicability to lipophilic drugs and Webb in particular teaches the advantages which relate to liposomes containing sphingomyelin and cholesterol themselves.

Applicant's arguments have been fully considered, but are not found to be moot in view of the new rejections.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615